Study of resting state cortico-cortical synchronization aimed to accurately discriminate Parkinson and essential tremor patients: A MEG source-space connectivity study

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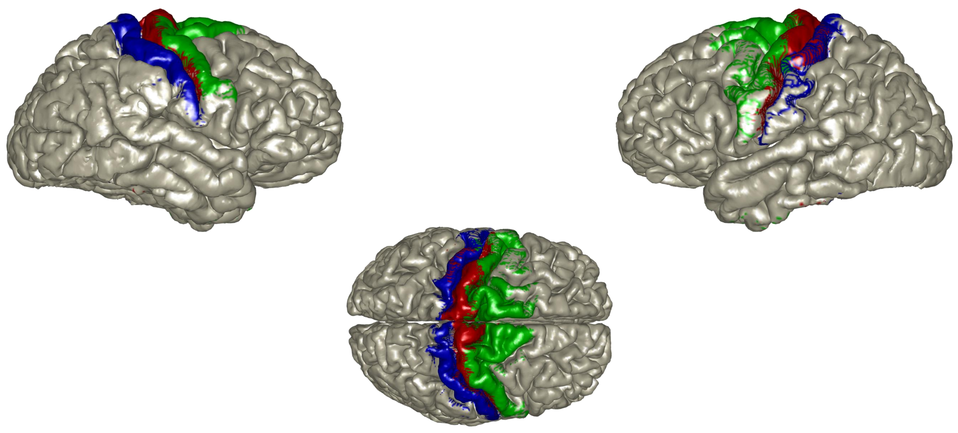
Introduction

Motor tremor-related syndromes like essential tremor (ET) and Parkinson's disease (PD) have a common symptomatology in early stages: the presence of tremor. Even when both diseases have a different aetiology and, thus, different prognosis and treatment, the symptoms in early stages are quite similar.

This usually leads to misdiagnosis, with the associated risks and limitations. A PD patient with an ET treatment will continue developing the disease, loosing an important window of action. On the other hand, an ET patient with a PD treatment will suffer strong side effects. A correct diagnosis is in both cases mandatory for the well-being of the patients.

In this experiment we tried to find a biomarker based in magneto-physiological data that allows clinicians a faster and easier diagnosis of ET and PD patients, saving time and money to both patients and hospitals.



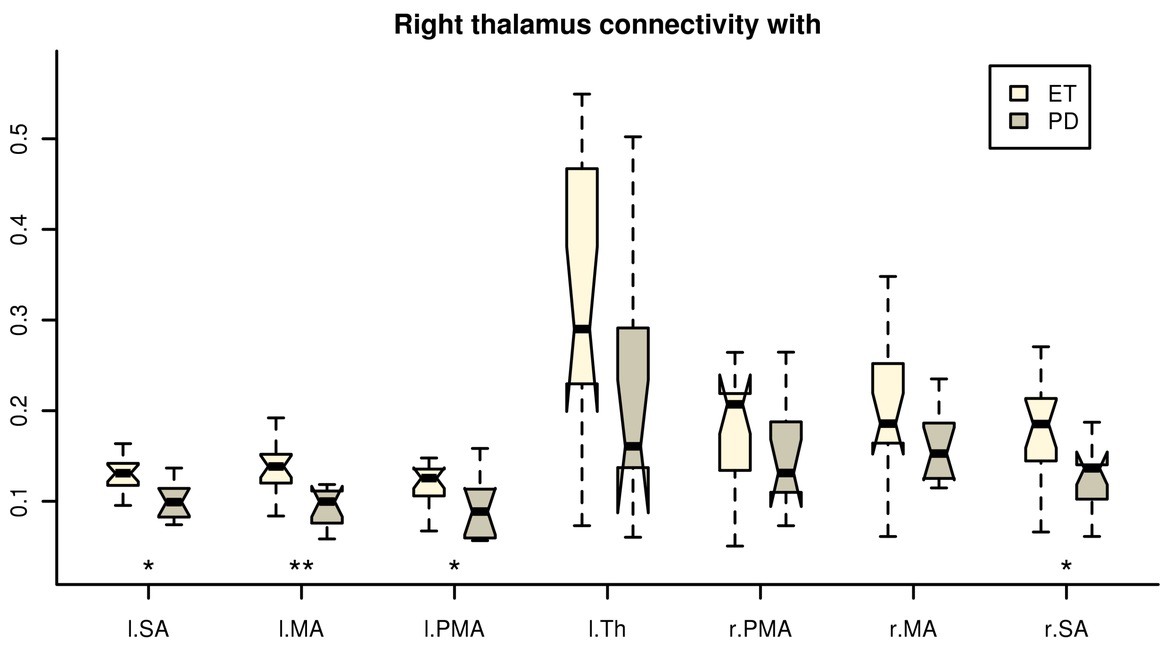
Cortical areas used as ROIs in this study: pre-motor area (PMA, green), primary motor area (MA, red) and somatosensory area (SA, blue).

Methods

For this study we used a sample of 28 patients from the neurology unit in Hospital 12 de Octubre, in Madrid. All the subjects were diagnosed as PD patients (11 subjects, 8 males, age 64.9 ± 10.8) or ET patients (17 subjects, 10 males , age 68.5 ± 12.1) after a thorough psychological and neurological evaluation. This evaluation was performed in the frame of the **NeuroTREMOR** project, an European Union-funded project aimed to correctly diagnose patients as ET or PD. The two groups of patients did not differ in age, gender or educational level.

The magnetoencephalographic (MEG) activity of the patients was recorded while 5 minutes with eyes open using an Elekta Neuromag whole head MEG system with 306 sensors, 102 magnetometers and 204 planar gradiometers, and a bipolar electrode was used to monitor cardiac activity. The data was movement-corrected using four head position indication coils and Elekta's commercial software *MaxMove*. A temporo-spatial signal separation filtering was also performed using Elekta's commercial software *MaxFilter*. The recorded MEG data was segmented in four seconds artefact-free epochs and the cardiac activity was removed using a independent component analysis-based procedure. Planar gradiometer's data were discarded due to coming from a composed sensor, and only the 102 magnetometers MEG data were used.

A source-space activity for the subjects was estimated using the MEG data and linearly constrained minimum variance beamformer, using a single-shell forward model calculated from the subject's T1 MRI image. As the study was performed in motor impaired patients, only some motor-related ROIs were used in the source reconstruction: thalamus (Th), primary motor area (MA), premotor area (PMA) and somatosensory area (SA) in each hemisphere, obtained using *FreeSurfer* software and the subject's T1 MRI. Four sources were placed distributed in the volume defined by each ROI, in order to capture all the possible information of the area. Then a between-ROI synchronization value was calculated between each pair of areas as the mean phase-locking value between each pair of sources in each area.



Results

Functional connectivity differed significantly ($p < 0.05$) between both groups. **The connections between the right thalamus and most of the cortical regions in both hemispheres were significantly stronger in ET patients** than in PD patients in the theta band. The boxplot showing the distributions of connectivity in theta band values are shown in the figure of the left.

Theta band shares frequencies with the tremor rhythm in all the patients evaluated in this study. These results seem to point out that the tremor in ET is, to some extent, caused by an excessive communication between thalamus and cortex.

In addition, functional connectivity between right thalamus and the cortical regions related to movement seems to be an interesting biomarker to discriminate PD and ET patients.

However, the sample is still small, and more data must be acquired to achieve a most definitive conclusion.